

REMARKS

Applicants respectfully request that the foregoing amendments be made prior to examination of the present application.

After amending the claims as set forth above, claims 1-18, 21-25, 28-30, 32 and 34 are now pending in this application.

Favorable consideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

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By

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**Version With Markings to Show Changes Made**

**Marked up rewritten claims:**

1. (Amended) A chemical compound of formula (I):

wherein:

R<sub>1</sub> to R<sub>3</sub> are independently selected from hydrogen and lower alkyl;

X<sub>1</sub> is selected from N and C-R<sub>4</sub>;

X<sub>2</sub> is selected from N and C-R<sub>5</sub>;

X<sub>3</sub> is selected from N and C-R<sub>6</sub>;

X<sub>4</sub> is selected from N and C-R<sub>7</sub>;

R<sub>4</sub>, R<sub>5</sub> and R<sub>7</sub> are independently selected from hydrogen, halogen, hydroxy, alkyl, aryl, alkoxy, aryloxy, alkoyl, aryloyl, alkylthio, arylthio, alkylsulfoxyl, arylsulfoxyl, alkylsulfonyl, arylsulfonyl, amino, alkylamino, dialkylamino, nitro, cyano, carboalkoxy, carboaryloxy and carboxy; and

R<sub>6</sub> is selected from hydrogen, halogen, alkyl, aryl, aryloxy, alkylthio, arylthio, alkylsulfoxyl, arylsulfoxyl, alkylsulfonyl, arylsulfonyl, amino, alkylamino, dialkylamino and cyano;

with the proviso that R<sub>4</sub> to R<sub>7</sub> are not all selected as hydrogen,

or a [and] pharmaceutically acceptable salt [salts], [and] addition compound or prodrug [compounds and prodrugs] thereof.

2. (Amended) A compound according to claim 1, wherein R<sub>1</sub> is selected from hydrogen and methyl.

3. (Amended) A compound according to claim 1 [or 2], wherein R<sub>2</sub> is hydrogen.

4. (Amended) A compound according to claim 1, [2 or 3] wherein  $R_3$  is selected from hydrogen and methyl.

5. (Amended) A compound according to [any preceding] claim 1, wherein  $X_2$  is C- $R_5$ .

6. (Amended) A compound according to [any preceding] claim 1, wherein  $X_3$  is C- $R_6$ .

7. (Amended) A compound according to [any preceding] claim 1, wherein  $X_4$  is C- $R_7$ .

8. (Amended) A compound according to [any preceding] claim 1, wherein  $X_1$  is C- $R_4$ .

9. (Amended) A compound according to [any preceding] claim 1, wherein two of  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  are hydrogen.

10. (Amended) A compound according to claim 9, wherein  $R_4$  and  $R_6$  are hydrogen.

11. (Amended) A compound according to [any of claims] claim 1 [to 8], wherein two of  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  are independently selected from hydrogen, chlorine, fluorine, trifluoromethyl and bromine.

12. (Amended) A compound according to [any of claims] claim 1 [to 8], wherein three of  $R_4$ ,  $R_5$ ,  $R_6$  and  $R_7$  are hydrogen.

13. (Amended) A compound according to claim 12, wherein  $R_4$ ,  $R_6$  and  $R_7$  are hydrogen.

14. (Amended) A compound according to [any of claims] claim 1 [to 8], wherein  $R_4$  is hydrogen.

15. (Amended) A compound according to [any of claims] claim 1 [to 8], wherein R<sub>5</sub> is halogen.

16. (Amended) A compound according to [any of claims] claim 1 [to 8], wherein R<sub>6</sub> is hydrogen.

17. (Amended) A compound according to [any of claims] claim 1 [to 8], wherein R<sub>7</sub> is halogen.

18. (Amended) A compound according to claim 1 which is selected from:

(*RS*) 7-chloro-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole,

(*R5*) 9-chloro-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole,

(*RS*) 7-chloro-8-methyl-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole,

(10a*R*) 7-chloro-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole,

(*RS*) 7-bromo-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole,

(3*S*, 10a*R*) 8-chloro-2-methyl-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole,

(10a*R*) 8-chloro-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole and

(3*S*, 10a*R*) 8-chloro-2-methyl-1,2,3,4,10,10a-hexahydropyrazino[1,2-*a*]indole.

21. (Amended) A method [use] according to claim 28 [20], wherein the disorders of the central nervous system are selected from depression, atypical depression, bipolar disorders, anxiety disorders, obsessive-compulsive disorders, social phobias or panic states, sleep disorders, sexual dysfunction, psychoses, schizophrenia, migraine and other conditions associated with cephalic pain or other pain, raised intracranial pressure, epilepsy, personality disorders, age-related behavioural disorders, behavioural disorders associated with dementia, organic mental disorders, mental disorders in childhood, aggressivity, age-related memory disorders, chronic fatigue

syndrome, drug and alcohol addiction, obesity, bulimia, anorexia nervosa and premenstrual tension.

22. (Amended) A method [use] according to claim 28 [20] wherein the damage to the central nervous system is by trauma, stroke, neurodegenerative diseases or toxic or infective CNS diseases.

23. (Amended) A method [use] according to claim 22, wherein said toxic or infective CNS disease is encephalitis or meningitis.

24. (Amended) A method [use] according to claim 28 [20], wherein the cardiovascular disorder is thrombosis.

25. (Amended) A method [use] according to claim 28 [20], wherein the gastrointestinal disorder is dysfunction of gastrointestinal motility.

28. (Amended) A method of treatment of disorders of the central nervous system; damage to the central nervous system; cardiovascular disorders; gastrointestinal disorders; diabetes insipidus, and sleep apnea, comprising administering to a patient in need of such treatment an effective dose of a compound of formula (I) as set out in [any one of claims] claim 1 [to 18].

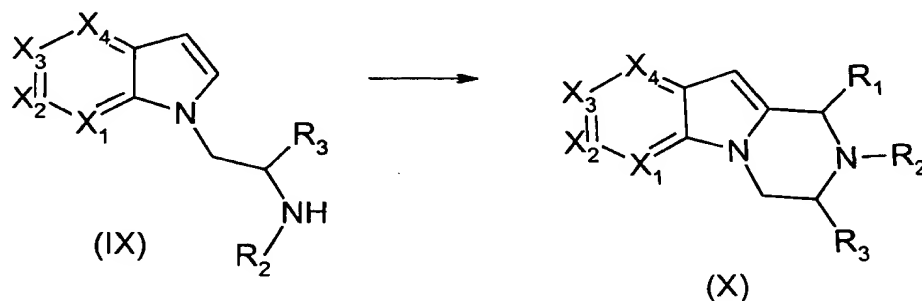
29. (Amended) A method of treatment according to claim 21 [28], wherein said disorder is obesity.

30. (Amended) A method according to claim 28 [or 29], wherein said treatment is prophylactic treatment.

32. (Amended) A pharmaceutical composition comprising a compound of formula (I) as set out in [any one of claims] claim 1 [to 18], in combination with a pharmaceutically acceptable carrier or excipient.

34. (Amended) A process for the preparation of a compound of formula (I) according to [any of claims] claim 1 [to 18], said process comprising the steps of:

(i) treating a compound of formula (IX) [as described herein] with an aldehyde of formula  $R_1CHO$ , and then exposing to acid to obtain a compound of formula (X), [as described herein] wherein  $X_1$ ,  $X_2$ ,  $X_3$ ,  $X_4$ ,  $R_2$  and  $R_3$  are as described in claim 1, and



(ii) reduction of a compound of formula (X).